STUDIES WITH IN VITRO DIAGNOSTIC DEVICES

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TOPICS

- Studies with unapproved/uncleared devices
- Terminology
- Conduct of studies
- Applicable regulations

NON-IVD DEVICE

IDEA

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PROTOTYPE DEVELOPMENT

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NON-CLINICAL STUDIES

↓

CLINICAL STUDIES

↓

SUBMISSION

IVD DEVICE

IDEA

↓

“COMPONENT” TESTING

↓

FEASIBILITY TESTING

↓

PERFORMANCE TESTING

↓

SUBMISSION

IVD Device Development

IDEA

R&D

“COMPONENT” TESTING

R&D + Investigators(?)

FEASIBILITY TESTING

Investigators

PERFORMANCE TESTING

IVD Device Development

IDEA

↓ Analytes;matrices;antibodies;etc.

“COMPONENT” TESTING

↓ Human tissue samples

FEASIBILITY TESTING

↓ Human tissue samples

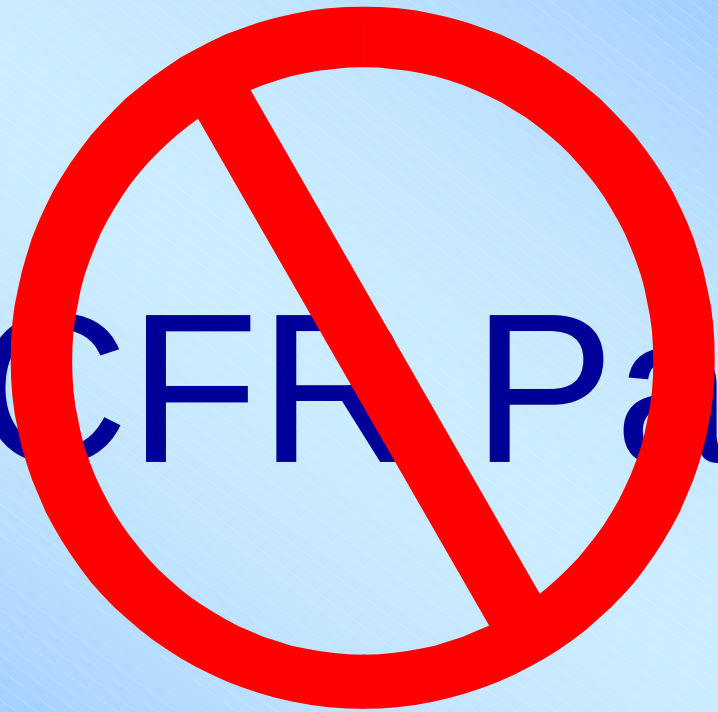
PERFORMANCE TESTING

TERMINOLOGY

NON-CLINICAL LABORATORY STUDY means in vivo or in vitro experiments in which test articles are studied prospectively in test systems under laboratory conditions ***to determine their safety*****. [21 CFR 58.3(d)]**

21 CFR Part 58 - GOOD LABORATORY PRACTICE FOR NONCLINICAL LABORATORY STUDIES

21 CFR Part 58



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TERMINOLOGY

INVESTIGATION means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device. **[21 CFR 812.3(h)]**

21 CFR Part 812 - INVESTIGATIONAL DEVICE EXEMPTIONS

TERMINOLOGY

SUBJECT means a human who participates in an investigation, either as an individual on whom ***or on whose specimen*** an investigational device is used or as a control. **[21 CFR 812.3(p)]**

TERMINOLOGY

"For Research Use Only. Not for use in diagnostic procedures." - labeling required for "a product in the laboratory research phase of development, and not represented as an effective in vitro diagnostic product" **[21 CFR 809.10(c)(2)(i)]**

21 CFR Part 809 - IN VITRO DIAGNOSTIC PRODUCTS FOR HUMAN USE

TERMINOLOGY

"For Investigational Use Only. The performance characteristics of this product have not been established." - labeling required for "a product being shipped or delivered for product testing prior to full commercial marketing."

[21 CFR 809(c)(2)(ii)]

"..in an attempt to substantiate the safety and effectiveness of a device, the agency relies upon only valid scientific evidence to determine whether there is reasonable assurance that the device is safe and effective." **[21 CFR 860.7(c)(1)]**

21 CFR Part 860 - MEDICAL DEVICE CLASSIFICATION PROCEDURES

CONDUCT OF STUDIES FDA EXPECTATIONS

- 21 CFR Part 812 = only device regulation that includes expectations regarding study conduct
- Many IVD studies are exempt from this regulation
- Varied nature of IVD studies

CONDUCT OF STUDIES FDA EXPECTATIONS

- Investigational plan
- Investigator qualifications/agreement
- Monitoring
- Data validation
- Records/Documentation
- Reports

CONDUCT OF STUDIES

IDEA

↓

"Investigational plan"; data validation; records

"COMPONENT" TESTING

↓

Investigational plan; data validation; records
[investigator qualifications/agreement;
monitoring; documentation; reports(?) - if investigator(s)]

FEASIBILITY TESTING

↓

Investigational plan; investigator qualifications/agreement;
monitoring; data validation; records/documentation; reports

PERFORMANCE TESTING

INVESTIGATIONAL PLAN

- Complexity dependent upon phase of development
- “Road map”
- Can be amended as needed
- If multiple investigators, all ***must*** have same version at the same time

REGULATIONS

21 CFR Part 820

QUALITY SYSTEM REGULATION (820.30 - Design Controls; 809.20(b) - IVDs manufactured according to GMPs in 820)

21 CFR Part 812

INVESTIGATIONAL DEVICE EXEMPTIONS

21 CFR Part 814

PREMARKET APPROVAL OF MEDICAL DEVICES

21 CFR Part 812

- Significant risk device study
  Full IDE requirements apply
- Non-significant risk device study
  Abbreviated IDE requirements in 812.2(b) apply
- Exempted from 21 CFR Part 812
  If 812.2(c)(3) conditions met

STUDIES EXEMPT FROM 21 CFR 812

- Diagnostic Test that is :
  - –non-invasive
  - –no significant risk invasive sampling procedure
  - –no energy introduced into subject
  - –not used as diagnostic procedure
- Labeling requirements in 21 CFR 809.10**(c)**
- 21 CFR Parts 50 and 56 apply

IDE STUDIES

- 1 or more of exemption criteria not met
- SR/NSR decision made on study particulars
- "Not used as diagnostic procedure" criteria "tricky"
  - accepted diagnostic must be part of any prospective study to be exempted
  - ethical concerns can change category

SIGNIFICANT RISK

If a device is:

- intended as an implant
- purported or represented as used in supporting or sustaining life
- of substantial importance in diagnosing, curing, mitigating, or treating disease or preventing impairment
- otherwise presents a potential for serious risk

and it presents a potential serious risk to the health, safety, and welfare of a subject

21 CFR PART 56 INSTITUTIONAL REVIEW BOARDS

An IRB

- needs to review ***all*** studies
- cannot waive review
- may use expedited review if minimal risk

21 CFR Part 50
PROTECTION OF HUMAN SUBJECTS

Interrelated Areas of Concern:

- Repository collections and research samples
- Identification of subjects

National Bioethics Advisory Commission (NBAC)

Report and Recommendations (August 1999):

Research Involving Human Biological Materials:

Ethical Issues and Policy Guidance

NBAC REPORT

- Concerns 45 CFR 46
- 21 CFR 56 governs FDA-regulated studies
- Concern for safety and welfare of study subjects
- Defines terms related to the identification of human biological materials

NBAC TERMINOLOGY

Repository Collections

Unidentified specimens - identifiable personal information not collected or not maintained and cannot be retrieved.

Identified specimens - linked to personal information in such a manner that the individual from whom the sample was obtained can be identified.

NBAC TERMINOLOGY

Research Samples

Unlinked samples - lack identifiers or codes that can link a particular sample to an identified specimen or particular person.

Coded samples - **"linked" samples** - from identified samples which can be traced back to the individual who supplied the sample

Identified samples - personal identifiers present which allow the researcher to directly access information on the individual who supplied the sample

INFORMED CONSENT

- Prospective studies; IRB-approved
- “Repository” sample collection
- Documentation for samples “bought”

RELATED ISSUES

- Information available relative to 510(k) & PMA submissions
- Privacy laws & other legal considerations
- State and local differences

CLINICAL TRIALS AND HUMAN SUBJECT PROTECTION

http://www.fda.gov/oc/health/hsp.html

CDRH BIMO WEB ADDRESS

http://www.fda.gov/cdrh/comp/bimo.html